REMARKS

Formal Matters

Claims 8-25 are pending.

Claims 8-25 were examined and rejected. No claims were allowed.

Claims 8 and 21-23 are amended. Support for the amendment to claims 8 and 21-23 is found in Fig. 2.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Interview Summary

The Applicants wish to express their gratitude to Examiner Brusca for the interview on June 6, 2005, with Applicants' representative James Keddie.

Exr. Brusca agreed that Fig. 2 supports recitation of a randomized amino acid sequence of up to 10 amino acids in length in the claims.

Rejection of claims under 35 U.S.C. § 103(a)

Claims 8-10, 12-19, 21 and 22 are rejected under 35 U.S.C. § 103(a) as unpatentable over Kauffman in view of Rayner and Gonda. The Office argues that Kauffman's screening methods, in combination with Rayner's retroviral vector and Gonda's N-terminal glycine, render the rejected claims obvious. The Applicants respectfully traverse this rejection.

Without any acquiescence to the correctness of this rejection and solely to expedite prosecution, the claims have been amended to recite test peptides that contain randomized amino acid sequence ***of up to 10 amino acids in length***.

Kauffman describes a method in which stochastically generated (interpreted to mean random by the Examiner) polynucleotide sequences are tested in cells to identify phenotype-altering polypeptides.

However, in contrast to what is being claimed, Kauffman's methods involving producing polypeptides that are considerably longer than 10 amino acids. Support for this assertion is found in Kauffman's col. 5 lines 28-51 and col. 6 lines 51-64, where Kauffman describes methods for making stochastically generated polynucleotides.

For example, at col. 5 lines 28-51 Kauffman's disclosure describes a first method in which a plasmid is linearized to produce a linear plasmid and nucleotides are sequentially added to the linear plasmid. According to the paragraph starting at line 40 of col. 5, the reaction is stopped when *at least 300 nucleotides* are added *to each of the 3'* ends of the linearized plasmid. Additional nucleotides (10-30 A nucleotides and 10-30 T nucleotides) are then added, and the plasmid is re-circularized. The final re-circularized plasmid thus contains at least 600 nucleotides encoding at least 200 contiguous amino acids. A polypeptide containing at least 200 contiguous amino acids is considerably larger than the peptides recited in the rejected claims.

Moreover, at col. 6 lines 51-64 Kauffman's disclosure describes a second method in which pre-synthesized 8-mer nucleotide oligomers are ligated together to form polymers containing at least 100 oligmers (col. 6, lines 62-65). The polymers are then ligated to form a linearized vector. Since each oligomer contains 8 nucleotides, and each polymer contains at least 100 oligomers, each polymer ligated to a linearized vector thus contains at least 800 nucleotides and encode at least 266 contiguous amino acids. A polypeptide containing at least 266 contiguous amino acids is considerably larger than the peptides recited in the rejected claims.

Kauffman neither describes nor suggests any method that employs "small" peptides such as those that are up to 10 amino acids in length. All discussion of the polypeptides generated in Kauffman points to making polypeptide that are much longer than10 amino acids.

In view of the above, the Applicants submit that Kauffman's disclosure is deficient in that it fails to disclose or fairly suggest any method that employs test peptides that contain up to 10 randomized amino acids.

Raynor, on the other hand, discloses a cellular assay in which *cDNAs* are introduced into cells that are then screened for a particular phenotype. Raynor, like Kauffman, is deficient because it fails to disclose or fairly suggest any method that employs test peptides that contain up to 10 randomized amino acids.

Gonda is cited to provide a polypeptide containing an N-terminal glycine. Gonda's disclosure is also deficient in that it fails to disclose or fairly suggest any method that employs test peptides that contain up to 10 randomized amino acids.

Raynor and Gonda therefore fail to meet the primary deficiency of Kauffman and, as such, the cited references, in combination, fail to disclose or fairly suggest an element of the rejected claims: a test peptide containing up to 10 randomized amino acids.

Since the cited prior art references fail to disclose or fairly suggest an element of the rejected claims, this rejection may be withdrawn.

Further to the above, the Applicants note that Rayner's disclosure is sharply focused on the identification of *cDNA-encoded proteins* that produce a particular phenotype. As would be recognized by one of skill in the art, cDNA-encoded proteins are derived from DNAs in the genome of a cell and have a specific biological activity. In order to provide this activity, cDNA-encoded proteins contain a defined, naturally-occurring sequence of amino acids. The amino acid sequence of a cDNA-encoded protein defines the activity of the protein.

In contrast to the cDNA-encoded proteins of Rayner, the rejected claims recite peptides having a *randomized* sequence of amino acids. Conceptually, such peptides are as far from those of cDNA-encoded protein as possible.

At no point does Rayner suggest methods for identifying proteins other than cDNA-encoded proteins. As such, Rayner provides no motivation to provide the claimed invention. In fact, Rayner's general teachings, in particular the phrase "retrovirus cloning can be used to isolate any **cDNA** for which a functional screen can be devised" (see Rayner's last paragraph; emphasis added) would lead one of skill in the art away from the invention. In other words, Rayner suggests that his method can be adapted for other situations where one *knows that a particular protein exists* and further *knows how to assay for that protein.* Rayner's suggestion would likely point one of skill in the art directly *away* from the claimed invention since, as discussed above, Rayner's cDNA-encoded proteins contain a *defined, ordered* sequence of amino acids and the claim-recited peptides contain a *random* sequence of amino acids. One need not know in advance that a random peptide exists that can elicit a desired effect on the cell. Indeed, the point of the claimed method is that it can be used to identify random peptides having a desired activity where the random peptides have no previously known function.

Further, Rayner's major focus is the identification of *cDNAs* that are *native*, i.e., endogenous, to the cell in which they are tested. It would take a major leap of imagination to substitute Rayner's cDNAs with Kauffman's randomized sequences since this would radically change the overall principle underlying Rayner's method.

In view of the foregoing discussion, this rejection may be withdrawn.

Claims 8 and 11 are rejected under 35 U.S.C. § 103(a) as unpatentable over Kauffman in view of Rayner, Gonda and Scott. The Office argues that Kauffman's screening methods, in combination with Rayner's retroviral vector, Gonda's N-terminal glycine and Scott's presentation structures, render the rejected claims obvious. The Applicants respectfully traverse this rejection.

As argued above, Kauffman, Rayner and Gonda are each deficient in that they fail to disclose or fairly suggest any method that employs test peptides that contain up to 10 randomized amino acids.

Scott's presentation structures fail to meet the deficiency of Kauffman, Rayner and Scott, and as such, this rejection fails to teach an element of each of the rejected claims: a method that employs test peptides that contain up to 10 randomized amino acids.

The Applicants respectfully request withdrawal of this rejection on this basis alone.

Further to the above, the Applicants note that Scott's disclosure is directed to random peptide libraries that are *cell-free* and contain *mixtures* of random peptides. Scott never reasonably suggests that a random peptide library is provided by expression from a cellular library, and never reasonably suggests any method in which a random peptide library may be screened using cells. Scott cannot be readily combined with Kauffman or Rayner because Scott's polypeptides are present as mixtures in a cell-free environment whereas the polypeptides of Kauffman and Rayner present in a cellular environment in which each cell contains a single type of polypeptide.

In view of the above, the Applicants submit that one of skill in the art would find no motivation to combine the methods of Kauffman, Rayner and Scott.

Claims 8, 19 and 20 are rejected under 35 U.S.C. § 103(a) as unpatentable over Kauffman in view of Rayner, Gonda and Garcia-Bustos. The Office argues that Kauffman's screening methods, in combination with Rayner's retroviral vector, Gonda's N-terminal glycine and Garcia-Bustos' nuclear localization sequence, render the rejected claims obvious. The Applicants respectfully traverse this rejection.

As argued above, Kauffman, Rayner and Gonda are each deficient in that they fail to disclose or fairly suggest any method that employs test peptides that contain up to 10 randomized amino acids.

Garcia-Bustos' nuclear localization sequence fails to meet the deficiency of Kauffman, Rayner and Scott, and as such, this rejection fails to teach an element of each of the rejected claims: a method that employs test peptides that contain up to 10 randomized amino acids.

In view of the foregoing discussion, the Applicants respectfully request withdrawal of this rejection.

Claims 23-25 are rejected under 35 U.S.C. § 103(a) as unpatentable over Kauffman in view of Rayner, Gonda and Abbas. The Office argues that Kauffman's screening methods, in combination with Rayner's retroviral vector, Gonda's N-terminal glycine and Abbas's B and T cell phenotypes, render the rejected claims obvious. The Applicants respectfully traverse this rejection.

As argued above, Kauffman, Rayner and Gonda are each deficient in that they fail to disclose or fairly suggest any method that employs test peptides that contain up to 10 randomized amino acids.

Abbas' phenotypes fail to meet the deficiency of Kauffman, Rayner and Scott, and as such, this rejection fails to teach an element of each of the rejected claims: a method that employs test peptides that contain up to 10 randomized amino acids.

In view of the foregoing discussion, the Applicants respectfully request withdrawal of this rejection.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-005CON.

Respectfully submitted,
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